Alzheimer's disease and gastrointestinal microbiota; impact of Helicobacter pylori infection involvement

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Abstract: Background: Alzheimer disease (AD) is a leading cause of global burden with great impact on societies. Although research is working intensively on promising therapy, the problem remains up-to-date. Among the various proposed hypotheses regarding causality and therapy, emerging evidence supports the hypothesis that gastrointestinal microbiota through the so-called 'gut-brain axis' interacts with immune system and brain and shape the balance between homeostasis and disease; the involvement of gastrointestinal microbiota in the pathophysiology of AD is less defined, even though the role of 'gut-brain axis' has been well verified for other neurodegenerative conditions.Methods: We performed a systematic review of PubMed/MEDLINE database from 1^{st} January 1990 to 17^{th} October 2018, to investigate the accessible literature regarding possible association between AD and gastrointestinal microbiota. Inclusion criteria were available full text in English language, original clinical papers implicating AD patients and any sort of gastrointestinal microbiota.Results: Through our query, an initial number of 241 papers has been identified. After removing duplicates and through an additional manual search, twenty-four papers met our inclusion criteria. The great majority of eligible publications supported a possible connection between AD and gastrointestinal microbiota. The most common investigated microorganism was Helicobacter pylori.Conclusion: Our own systematic review, showed a possible association between AD and gastrointestinal microbiota mainly including Helicobacter pylori, and thus further research is required for substantiation of causality as well as for the establishment of promising novel therapies.

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Table 1. Demographics of included studies

Authors (Year)	Country	Type of study	Number of patients (control group)	Gender f, m (control f,m)	Mean age in years (control group)	Follow up in months
Akbari et al. (2016)	Iran	Randomized controlled trial	30 (30)	24,6	77 (82)	3
Andreadou et al. (2017)	Greece	Prospective cohort study	9 (9) [serum] 21 (7) [CSF]	5,4 (4,5) [serum] 10,11 (3,4) [CSF]	75 (70) [serum] 74 (76) [CSF]	NM NM
Araos et al. (2018)	Chile / USA	Retrospective cohort study	7 (21)	**21,7 (total cases n=28)**	**89 (total cases n=28)**	12
Beydoun et al. (2013)	USA	Cross sectional study	2438 (3382)	1243, 1195 (NM)	36 (70)	NM
Bu et al. (2015)	China	Case control study	128 (135)	69, 59 (63,72)	70 (69)	NM
Cattaneo et al. (2017)	UK,CH, Italy	Cross-sectional	40 (33) (10)	20,20 [18,15] (6,4)	71 (70) (68)	NM
Farhad et al. (2014)	Iran	Case control study	40 (40)	NM	NM	NM
Ide et al. (2016)	UK	Prospective cohort study	22 (37)	9,13 (20,17)	75 (79)	6
Katan et al. (2013)	USA	Prospective cohort study	1625	1054, 571	69	12
Kountouras et al. (2006)	Greece	Prospective cohort study	50 (30)	32,18, (16,14)	65 (62)	NM
Kountouras et al. (2007)	Greece	Prospective cohort study	63 (35)*	41,22 (18,17)	66 (68)	NM
Kountouras et al. (2009)	Greece	Prospective cohort study	27 (27)*	15,12 (18,9)	(70,72)	NM
Kountouras et al. (2009)	Greece	Prospective cohort study	50 (30)*	32,18 (16,14)	65 (62)	24
Kountouras et al. (2010)	Greece	Prospective cohort study	46	30,16	73	60
Mahami-Oskouei et al. (2016)	Iran	Case-control study	75 (75)	41, 34 (NM)	76 (76)	NM
Malaguarnera et al. (2004)	Italy	Case-control study	30 (30) (30)	13,17 [20,10] (17,13)	75 [71] (74)	NM
Meer-Scherrer et al. (2006)	USA	Case-control study	1	1,0	83	NM
Nägga et al. (2003)	Sweden	Case-control study	126 (101)*	76 (50) (49,52)	76 (69)	NM
Noble et al. (2014)	USA, Greece	Retrospective cohort study	110 (109)	75, 35 (73,36)	79 (72)	60
Roubaud-Baudron (2012)	France	Retrospective cohort study	53	30,23	69	NM
Roubaud-Baudron (2013)	France	Prospective cohort study	603	348,255	74	every 24-36
Shiota et al. (2011)	Japan	Case-control study	385 (97)	271,114 (80,17)	79 (70)	NM
Sparks Stein et al. (2012)	USA	Retrospective case-control study	46 (35) (77)	22,24 [26,9] (45,32)	72 (74) (70)	144
Zhan et al. (2016)	USA	Case-control study	24 (18)	15,9 (8,10)	77 (81)	NM

Table 1 legend: * consecutive patients, CD: Clostridium Difficile, CSF: cerebrospinal fluid, HP: *Helicobacter pylori*, IBS: Irritable Bowel Syndrome, LPS: lipopolysaccharides, MCI: Mild Cognitive Impairment, NM: not mentioned, yo: years old